

~~107. The method of claim 105, wherein removal of one α 1,3 mannose residue distal to the pentasaccharide core is prevented.~~

~~108. The method of claim 105, wherein removal of one α 1,6 mannose residue distal to the pentasaccharide core is prevented.~~

109. The method of claim 105, wherein the kifunensine is present at a concentration between about 0.05 to 20.0 $\mu\text{g/ml}$.

110. The method of claim 109, wherein the kifunensine is present at a concentration between about 0.1 to 2.0 $\mu\text{g/ml}$

111. The method of claim 105, further comprising contacting the cell with a class 2 processing mannosidase inhibitor.

112. The method of claim 111, wherein the class 2 processing mannosidase inhibitor is selected from the group consisting of: swainsonine, mannostatin, 6-deoxy DIM, 6-deoxy-6-fluoro-DIM and combinations thereof.

113. The method of claim 111, wherein the class 2 processing mannosidase inhibitor is swainsonine.

114. The method of claim 111, wherein the class 2 processing mannosidase inhibitor is present at a concentration between 0.05 to 20.0 $\mu\text{g/ml}$.

115. The method of claim 105, wherein the hmGCB has at least one carbohydrate chain having five mannose residues.

116. The method of claim 105, wherein the hmGCB has at least one carbohydrate chain having eight mannose residues.

117. The method of claim 105, wherein the hmGCB has at least one carbohydrate chain having nine mannose residues.

118. The method of claim 105, wherein the removal of one or more mannose residues distal to the pentasaccharide core is prevented on at least two carbohydrate chains of hmGCB.

119. The method of claim 105, wherein at least 60% of the hmGCB of the preparation have one or more carbohydrate chains in which the removal of one or more mannose residues distal to the pentasaccharide core has been prevented.

120. The method of claim 119, wherein the removal of three or more mannose residues distal to the pentasaccharide core has been prevented.

121. The method of claim 105, wherein at least about 20% of the hmGCB of the preparation have one or more carbohydrate chains having at least eight mannose residues.

122. The method of claim 121, wherein at least about 40% of the hmGCB of the preparation have one or more carbohydrate chains having at least eight mannose residues.

123. The method of claim 122, wherein at least about 60% of the hmGCB of the preparation have one or more carbohydrate chains having at least eight mannose residues.

124. The method of claim 105, wherein at least about 80% or more of the carbohydrate chains of the hmGCB preparation have six or more mannose residues.

125. The method of claim 105, wherein the cell is a knockout for at least one class 2 processing mannosidase.

126. The method of claim 105, wherein the cell comprises a class 2 processing mannosidase antisense molecule.

127. The method of claim 105, wherein the cell comprises an exogenous nucleic acid sequence comprising a GCB coding region.

128. The method of claim 127, wherein the cell further comprises an exogenous regulatory sequence which functions to regulate expression of the GCB coding region.

129. The method of claim 105, wherein the cell comprises an exogenous regulatory sequence which functions to regulate expression of an endogenous GCB coding sequence.

130. The method of claim 105, wherein the cell is a primary cell.

131. The method of claim 105, wherein the cell is a secondary cell.

132. The method of claim 105, wherein the cell is a mammalian cell

133. The method of claim 132, wherein the cell is a human cell.

134. The method of claim 133, wherein the cell is a fibroblast or a myoblast.

135. The method of claim 133, wherein the cell is an immortalized cell.

136. The method of claim 134, wherein the cell is an HT-1080 cell.

137. The method of claim 105, wherein the cell is contacted with kifunensine in culture media.

138. The method of claim 137, wherein the hmGCB is obtained from the media in which the cell is cultured.

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~~139. A method of producing high mannose glucocerebrosidase (hmGCB), comprising:
providing a cell into which a nucleic acid sequence comprising an exogenous regulatory sequence has been introduced such that the regulatory sequence regulates the expression of an endogenous GCB coding region;
contacting the cell with a substance which prevents the removal of at least one mannose residue distal to the pentasaccharide core of a precursor oligosaccharide of GCB; and
allowing the cell to produce hmGCB, to thereby produce an hmGCB preparation.~~

140. The method of claim 139, wherein removal of one or more α 1,2 mannose residue(s) distal to the pentasaccharide core is prevented.

Claim 139
141. The method of claim 139, wherein removal of one α 1,3 mannose residue distal to the pentasaccharide core is prevented.

142. The method of claim 139, wherein removal of one α 1,6 mannose residue distal to the pentasaccharide core is prevented.

143. The method of claim 139, wherein the substance is a class 1 processing mannosidase inhibitor.

144. The method of claim 143, wherein the class 1 processing mannosidase inhibitor is kifunensine.

145. The method of claim 144, wherein the kifunensine is present at a concentration between about 0.05 to 20.0 μ g/ml.

146. The method of claim 145, wherein the kifunensine is present at a concentration between about 0.1 to 2.0 $\mu\text{g/ml}$.

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147. The method of claim 144, further comprising contacting the cell with a class 2 processing mannosidase inhibitor.

148. The method of claim 147, wherein the class 2 processing mannosidase inhibitor is selected from the group consisting of: swainsonine, mannostatin, 6-deoxy DIM, 6-deoxy-6-fluoro-DIM and combinations thereof.

149. The method of claim 147, wherein the class 2 processing mannosidase inhibitor is swainsonine.

150. The method of claim 147, wherein the class 2 processing mannosidase inhibitor is present at a concentration between 0.05 to 20.0 $\mu\text{g/ml}$.

151. The method of claim 139, wherein the cell is a knockout for at least one class 2 processing mannosidase.

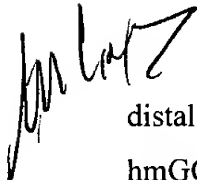
152. The method of claim 139, wherein the cell comprises a class 2 processing mannosidase antisense molecule.

153. The method of claim 139, wherein the hmGCB has at least one carbohydrate chain having six mannose residues of the precursor oligosaccharide.

154. The method of claim 139, wherein the hmGCB has at least one carbohydrate chain having eight mannose residues of the precursor oligosaccharide.

155. The method of claim 139, wherein the hmGCB has at least one carbohydrate chain having nine mannose residues of the precursor oligosaccharide.

156. The method of claim 139, wherein the substance prevents removal of at least three mannose residues distal to the pentasaccharide core of the precursor oligosaccharide of GCB.

 157. The method of claim 139, wherein the removal of one or more mannose residues distal to the pentasaccharide core is prevented on at least two of the carbohydrate chains of hmGCB.

158. The method of claim 139, wherein at least 60% of the hmGCB of the preparation have one or more carbohydrate chains in which the removal of three or more mannose residues distal to the pentasaccharide core has been prevented.

159. The method of claim 139, wherein at least 20% of the hmGCB of the preparation have one or more carbohydrate chains having at least eight mannose residues.

160. The method of claim 159, wherein at least 40% of the hmGCB of the preparation have one or more carbohydrate chains having at least eight mannose residues.

161. The method of claim 160, wherein at least 60% of the hmGCB of the preparation have one or more carbohydrate chains having at least eight mannose residues.

162. The method of claim 139, wherein at least about 80% or more of the carbohydrate chains of the hmGCB preparation have six or more mannose residues.

163. The method of claim 139, wherein the cell is a primary cell.

164. The method of claim 139, wherein the cell is a secondary cell.

165. The method of claim 139, wherein the cell is a mammalian cell
166. The method of claim 165, wherein the cell is a human cell.
167. The method of claim 166, wherein the cell is a fibroblast or a myoblast.
168. The method of claim 166, wherein the cell is an immortalized cell.
169. The method of claim 168, wherein the cell is an HT-1080 cell.
170. The method of claim 144, wherein the cell is contacted with kifunensine in culture media.
171. The method of claim 170, wherein the hmGCB is obtained from the media in which the cell is cultured.
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172. A high mannose glucocerebrosidase (hmGCB) preparation, wherein each hmGCB has four carbohydrate chains and wherein at least about 10% of the carbohydrate chains in the hmGCB preparation have six or more mannose residues of a precursor oligosaccharide.
173. The hmGCB preparation of claim 172, wherein at least about 30% of the carbohydrate chains in the hmGCB preparation have six or more mannose residues of a precursor oligosaccharide.
174. The hmGCB preparation of claim 173, wherein at least about 60% of the carbohydrate chains in the hmGCB preparation have six or more mannosidase residues of a precursor oligosaccharide.
175. The hmGCB preparation of claim 172, wherein at least about 10% of the carbohydrate chains in the hmGCB preparation have eight or more mannose residues of a precursor oligosaccharide.

176. The hmGCB preparation of claim 175, wherein at least about 30% of the carbohydrate chains in the hmGCB preparation have eight or more mannose residues of a precursor oligosaccharide.

177. The hmGCB preparation of claim 176, wherein at least about 60% of the carbohydrate chains in the hmGCB preparation have eight or more mannose residues of a precursor oligosaccharide.

178. A high mannose glucocerebrosidase (hmGCB) comprising at least one carbohydrate chain having six or more mannose residues of a precursor oligosaccharide.

179. The hmGCB of claim 178, wherein at least two carbohydrate chains having six or more mannose residues of a precursor oligosaccharide.

180. The hmGCB of claim 179, wherein the carbohydrate chain has eight or more mannose residues of a precursor oligosaccharide.

181. A pharmaceutical composition, comprising:
the hmGCB preparation of any of claims 172-180, in an amount suitable for treating
Gaucher disease.

182. The composition of claim 181, further comprising a pharmaceutically acceptable carrier or diluent.

183. A method of treating a subject having Gaucher disease, comprising:
administering to the subject the composition of claim 181, to thereby treat Gaucher
disease.
